Enhanced Brainstem Cerebral Blood Flow Accompanies Symptoms of Anhedonia in Young Adults

Simona Graur, Henry W. Chase, Tae Kim, Richelle Stiffler, Tsafrir Greenberg, Haris Aslam, Jeanette C. Lockovich, Genna Bebko, Mary L. Phillips

Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA

BACKGROUND
- Midbrain monoaminergic projections – including dorsal raphe nucleus (DRN), locus coeruleus (LC)1, and ventral tegmental area (VTA) are of crucial theoretical significance for mood disorders
- Learned helplessness associated with enhanced metabolic activity in the midbrain (dorsal raphe) of rodents2
- However, little human neuroimaging evidence supports involvement of monoaminergic projections in illness severity prediction
- Present study: Arterial Spin Labelling (ASL) promising tool to examine enhanced Blood flow was measured via multiband pseudo continuous ASL sequence

METHODS

Participants
36 distressed (DS) and 34 healthy controls (HC)

Resting State Acquisition
Participants told to relax and watch fixation cross for six minutes

Neural Measures
- Blood flow was measured via multiband pseudo continuous ASL sequence
- Regional cerebral perfusion data was collected with 25 slices, multiband factor=5, 4mm slice thickness, FA=90, 64x64 resolution FOV=192x912, TR/TE=3.5s/19ms, labeling time=1.5s and postlabeling delay=1.7s.
- Data was processed using Statistical Parametric Mapping (SPM)

RESULTS

Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>DS</th>
<th>HC</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>22.2 ± 2.1</td>
<td>21.5 ± 1.8</td>
<td>t(68)=2.84, p&lt;0.001</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>9/27</td>
<td>15/19</td>
<td>T&lt;1</td>
</tr>
<tr>
<td>SES</td>
<td>5.3 ± 1.1</td>
<td>5.5 ± 1.1</td>
<td>T&lt;1</td>
</tr>
</tbody>
</table>

Clinical Measures

- Anhedonia measured via: Mood and Anxiety Symptom Questionnaire Anhedonic Depression Scale (MASQ-ADS) and Snait–Hamilton Pleasure Scale (SHAPS) as a secondary measure
- Anxiety measured via: Mood and Anxiety Symptom Questionnaire General Distress Anxious Symptoms Scale (MASQ GD-A)

Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>DS</th>
<th>HC</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASQ-AD</td>
<td>75.6 ± 16.6</td>
<td>50.3 ± 9.1</td>
<td>t(68)=7.9, p&lt;0.001</td>
</tr>
<tr>
<td>SHAPS</td>
<td>27.8 ± 7.8</td>
<td>18.9 ± 5.2</td>
<td>t(68)=6.7, p&lt;0.001</td>
</tr>
<tr>
<td>MASQ GD-A</td>
<td>28.0 ± 10.1</td>
<td>13.5 ± 2.1</td>
<td>t(68)=8.2, p&lt;0.001</td>
</tr>
</tbody>
</table>

Clinical Measures

- Anhedonia measured via: Mood and Anxiety Symptom Questionnaire Anhedonic Depression Scale (MASQ-ADS) and Snait–Hamilton Pleasure Scale (SHAPS) as a secondary measure
- Anxiety measured via: Mood and Anxiety Symptom Questionnaire General Distress Anxious Symptoms Scale (MASQ GD-A)

Participants told to relax and watch fixation cross for six minutes

Association between anhedonia and midbrain CBF, with increasing endorsement of anhedonic symptoms predicting enhanced CBF

Figure 1 and 2 show regions positively correlating with individual differences in anhedonia (threshold uncorrected p<0.001).

Peak voxels within the midbrain located bilaterally (left: T=5.24, p_FWE=.033, x=-12, y=-34, z=-26; right: T=4.96, p_FWE=.080, x=9, y=-34, z=-23).

CONCLUSION

- Anhedonia associated with altered CBF in the midbrain in a young adult population showing heterogeneous symptoms of distress.
- Anhedonia associated with increased CBF in midbrain, possibly the LC.
- If key region is in fact LC, current findings link noradrenergic projections and anhedonia in humans, consistent with prior experimental studies of the effect of noradrenergic agents on the human reward system3.

Future Directions
- ASL promising tool to examine enhanced local perfusion, potentially reflecting underlying midbrain serotonergic activity
- Learned helplessness studies in rodents show similar findings2, but has thus far been difficult to investigate in humans.

Limitations
- Better resolution is needed to differentiate between relatively small midbrain structures
- No behavioral measure of anhedonia to link with animal work

REFERENCES

Acknowledgments: the present work was supported by NIMH grant MH100041 “Reward, pathophysiological dimensions and psychological distress in young adults” (PI: Mary Phillips, MD)